Circulatory System Devices Panel
Questions for Discussion

PercuSurge GuardWire System
K003992

February 5, 2001

Question #1
The randomized study was divided into two phases that may be considered two randomized clinical trials (RCT). The sponsor has designated the two phases as RCT-1 and RCT-2. RCT-1 consisted of 142 patients and RCT-2 consisted of 551 patients. The criteria for the lesions in the SVG were different in these two RCT phases. The patient selection criteria for RCT-1 required that the patients have a maximum of two lesions within a single saphenous vein graft which required treatment. The patient selection criteria for RCT-2 required that the patients have one or more lesions within a single saphenous vein graft, located in the proximal segment (at least 5 mm distal to the proximal anastomotic site), mid-body segment and distal segment (at least 20 mm proximal to the distal anastomotic site) which required treatment. The intent of this change was to allow more complex, multiple or diffuse lesions to be treated in RCT-2.

1. Please discuss whether there are any substantial differences in the lesions treated in RCT-1 and RCT-2 that could affect the poolability of the data.

Question #2

A substantial difference in 30-day MACE rates was noted in the control arm of the SAFER Trial after inclusion/exclusion criteria were modified. After the entry criteria were changed the control MACE rate increased from 10% to 20%. Review of demographic and angiographic data between RCT-1 and RCT-2, however, did not suggest major differences in the populations being studied.

Table 1. Patient Baseline Demographic and Clinical Characteristics

	RCT-1		RCT-2	
	GuardWire	Control	GuardWire	Control
Number of Patients	72	70	273	278
Average Age (years)	68.0	69.1	68.2	68.5
Number of Men	61/72 = 84.7%	58/70 = 82.9%	219/272 = 80.5%	236/278 = 84.9%
Hypertension	56/72 = 77.8%	58/69 = 84.1%	199/272 = 73.2%	201/276 = 72.8%
Hyperlipidemia	57/72 = 79.2%	51/70 = 72.9%	199/272 = 73.2%	197/277 = 71.1%
Current Smoker	4/71 = 5.6%	4/69 = 5.8%	29/268 = 10.8%	30/270 = 11.1%
Diabetes Mellitis	28/72 = 38.9%	21/69 = 30.4%	87/273 = 31.9%	98/278 = 35.3%
PVD	17/72 = 23.6%	16/70 = 22.9%	58/271 = 21.4%	57/277 = 20.6%
Prior MI	47/69 = 68.1%	50/70 = 71.4%	159/266 = 59.8%	172/270 = 63.7%
Prior CVA or TIA	12/72 = 16.7%	8/70 = 11.4%	30/272 = 11.0%	36/275 = 13.1%
Stable Angina	3/72 = 4.2%	3/70 = 2.9%	16/272 = 5.9%	16/276 = 5.8%
Worsening Angina	32/72 = 44.4%	28/70 = 40.0%	109/272 = 40.1%	110/276 = 39.9%
Rest Angina	26/72 = 36.1%	34/70 = 48.6%	105/272 = 38.6%	102/276 = 37.0%
No Angina	4/72 = 5.6%	6/70 = 8.6%	22/272 = 8.1%	23/276 = 8.3%
CCS III or IV	56/72 = 77.8%	62/70 = 88.6%	202/270 = 73.8%	206/276 = 74.6%
Single Vessel Disease	6/71 = 8.5%	3/69 = 4.3%	13/266 = 4.9%	14/276 = 5.1%
Two Vessel Disease	12/71 = 16.9%	12/69 = 17.4%	57/266 = 21.4%	41/276 = 14.9%
Three Vessel Disease	53/71 = 73.6%	54/69 = 78.3%	196/266 = 73.3%	221/276 = 80.1%
Average LVEF	46.4%	45.6%	48.3%	47.0%

Table 2. Lesion Baseline Characteristics

	RCT-1		RCT-2	
	GuardWire	Control	GuardWire	Control
Number of Lesions	78	78	295	302
Mean RVD (mm)	3.35	3.39	3.45	3.47
Mean MLD (mm)	1.09	1.12	1.08	1.05
Mean %DS	67.0%	66.9%	69.0%	70.1
Mean LL (mm)	14.92	15.97	15.83	17.43
SVG to LAD	17/76 = 22.4%	18/75 = 24.0%	52/264 = 19.7%	47/276 = 17.0%
SVG to LCX	36/76 = 47.4%	35/75 = 46.7%	113/264 = 42.8%	114/276 = 41.3%
SVG to RCA	23/76 = 30.3%	22/75 = 29.3%	98/264 = 37.1%	115/276 = 41.7%
Calcified	1/76 = 1.3%	3/75 = 4.0%	67/264 = 25.4%	66/276 = 23.9%
Thrombus	29/75 = 38.7%	29/75 = 38.7%	102/264 = 38.6%	106/276 = 38.4%
Eccentric	24/75 = 32.0%	24/75 = 32.0%	99/263 = 37.6%	94/276 = 34.1%
Angulated > 45 Degrees	2/76 = 2.6%	4/75 = 5.3%	17/263 = 6.5%	17/276 = 6.2%
ACC/AHA Lesion Class				
A	5/76 = 6.6%	20/75 = 13.3%	12/264 = 4.5%	14/276 = 5.1%
B1	18/76 = 23.7%	18/75 = 24.0%	47/264 = 17.8%	50/276 = 18.1%
B2 or Higher	36/76 = 47.4%	33/75 = 44.0%	147/264 = 55.7%	140/276 = 50.7%
C	17/76 = 22.4%	14/75 = 18.7%	58/264 = 22.0%	72/276 = 26.1%

2. Please comment on this difference in control results. Are there any other methods that should be used to assess interventional risk in a diseased SVG graft?

Question #3

A total of 1104 patients were enrolled in the study. The submission includes data collected for 979 subjects (286 roll-in subjects and 693 randomized subjects). Five hundred and fifty one of the randomized subjects were enrolled after a change to the inclusion criteria and are the basis of the primary analysis. Of the 551 subjects, 273 were randomized to the Guardwire arm and 278 were randomized to the control arm. The data presented are based on an interim analysis and do not include subjects that were enrolled near the end of the trial. Although several interim analyses were planned in the study protocol, these analyses were not executed as originally designed and the FDA has not formally agreed to the sponsor's revised analysis plan in which the first 142 patients enrolled in the trial are excluded from the primary analysis.

3. Considering both the planned a priori and realized post hoc interim looks at these data, do you have any recommendations regarding the following questions:

- **Please discuss the Type I error values that should be associated with each planned or realized look. These values must assure an overall study Type I error of 0.05. Their values may not only impact the results of hypotheses tests but may also change the widths of the reported confidence intervals. These changes could influence the evaluation process and the labeling.**
- **Please discuss whether the 142 patients enrolled prior to the change in the inclusion criteria should be included in the primary analysis. If not, which patient cohort should be the primary analysis cohort?**

Question #4

Table 7 of the SAFER Clinical Report (page 36) and the Narrative Summaries (pages 37-88) identifies the device failures and malfunctions that occurred during the study.

4. Please discuss the clinical importance of the device failure and malfunction events in the evaluation of the safety and effectiveness of the GuardWire System.

Question #5

5. Based on the data submitted by the applicant please discuss whether the benefits of the distal protection device in this patient population outweigh the risks associated with the use of this device.

Product Labeling

Question #6

One aspect of the premarket evaluation of a new product is the review of its labeling. The labeling must indicate which patients are appropriate for treatment, identify the products potential adverse events, and explain how the product should be used to maximize benefits and minimize adverse effects. Please address the following questions regarding the product labeling (Section 2):

6a. Based on the data from RCT-1 and RCT-2 as discussed in question 2, do you recommend that the Percusurge device be labeled for use in all SVG lesions? Please comment on the INDICATIONS FOR USE section (page 2) as to whether it identifies the appropriate patient population for treatment with the device.

6b. Please comment on the CONTRAINDICATIONS as to whether there are conditions under which the device should not be used because the risk of use clearly outweighs any possible benefit.

6c. Please comment on the WARNINGS and PRECAUTIONS sections as to whether it identifies all potential hazards regarding device use.

6d. Please discuss whether any improvements could be made to the labeling to help minimize the occurrence of device failures and malfunctions as discussed under question 4.

6e. Please comment on the remainder of the device labeling as to whether it adequately describes how the device should be used to maximize benefits and minimize adverse events.

6f. Do you have any other recommendations regarding the labeling of the device?

Training Program

Question #7
A summary of the Physician Training Program has been provided in Section 7

7a. Please discuss any improvements that could be made to the training program to help minimize the occurrence of device failures and malfunctions as discussed under question 4.

7b. Please identify any other important elements that should be contained in a physicians training program for this device.